

REMARKS

In the Office Action, the Examiner rejected claims 22-53. In view of the following remarks, Applicants respectfully request reconsideration and allowance of all pending claims.

Claim Rejections under 35 U.S.C. § 112, Second Paragraph

The Examiner rejected claims 22-39, 43-48 and 50 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Legal Precedent and Guidelines

The essential inquiry pertaining to the definiteness requirement is whether the claims set out and circumscribe a particular subject matter with a reasonable degree of clarity and particularity. See M.P.E.P. § 2173.02. As set forth in Section 2173 of the Manual of Patent Examining Procedure, definiteness of claim language must be analyzed, not in a vacuum, but in light of:

- (A) The content of the particular application disclosure;
- (B) The teachings of the prior art; and
- (C) The claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made.

In reviewing a claim for compliance with 35 U.S.C. 112, second paragraph, the examiner must consider the claim as a whole to determine whether the claim apprises one of ordinary skill in the art of its scope and, therefore, serves the notice function required by 35 U.S.C. 112, second paragraph, by providing clear warning to others as to what constitutes infringement of the patent. See *Solomon v. Kimberly-Clark Corp.*, 216 F.3d 1372, 1379, 55 U.S.P.Q.2d 1279, 1283 (Fed. Cir. 2000). Only when a claim remains insolubly ambiguous without a discernible meaning after all reasonable attempts at construction must a court declare it indefinite. See *Metabolite Labs., Inc. v. Lab. Corp. of Am. Holdings*, 370 F.3d 1354, 1366, 71 U.S.P.Q.2d 1081, 1089 (Fed. Cir. 2004). The

Examiner is also reminded not to equate breadth of a claim with indefiniteness. *In re Miller*, 441 F.2d 689, 169 U.S.P.Q 597 (CCPA 1971).

Rejection of Claims 22-39, 43-48 and 50 under 35 U.S.C. § 112, Second Paragraph

In rejecting claims 22-39, 43-48 and 50 the Examiner stated that “the phrase ‘intercalating moiety is configured to insert into the structure of deoxyribonucleic acid’ recited in claims 22 and 32 is a relative term which renders the claim indefinite.” Office Action, p. 3. Applicants respectfully disagree with the Examiner and request reconsideration.

The phrase “the intercalating moiety is configured to insert into the structure of deoxyribonucleic acid” is a definite phrase that clearly indicates that the precursor species used to synthesize the intercalating moiety is chosen in such a way as to functionally insert into the structure of DNA. The phrase is not a relative term or a term of degree, as described in MPEP §2173.05(b). It is, instead, a functional limitation that indicates the specific function that the “intercalating moiety” performs. As noted in MPEP §2173.05(g), “a functional limitation must be evaluated and considered, just like any other limitation of the claim, for what it fairly conveys to a person of ordinary skill in the pertinent art in the context in which it is used.” See *Innova/Pure Water Inc. v. Safari Water Filtration Sys. Inc.*, 72 USPQ2d 1001, 1006-1008 (Fed. Cir. 2004). Further, courts have held that such language as “adapted to be” serves to precisely define present structural attributes. *In re Venezia*, 189 USPQ 149 (CCPA 1976) (in which the court held that the phrase “members adapted to be positioned” was not indefinite). Accordingly, the phrase “is configured to insert into the structure of deoxyribonucleic acid” precisely defines a structural attribute of the “intercalating moiety,” namely the ability to insert into the structure of DNA.

Furthermore, the references provided with the previous Response (filed on December 20, 2007), Long and Lerman, illustrate that one of ordinary skill in the art at the time of filing of the application would understand the definition of an “intercalating moiety.” Moreover, while these references show that the term “intercalating moiety” clearly carries the definition that the moiety involved will insert between the base pairs in

the ladder structure of DNA, the claims make this even clearer by reciting that the moiety is functionally “configured to insert into the structure of deoxyribonucleic acid.” Independent claims 22 and 32 were also amended in the previous Amendment filed on December 20, 2007, to clarify the specific structural features, reciting “wherein the intercalating moiety comprises at least one unsubstituted aromatic ring that shares two carbons with only one other aromatic ring.” Therefore, the claims clearly define the scope. As noted in the legal precedent section above, only when a claim remains insolubly ambiguous without a discernible meaning after all reasonable attempts at construction must a court declare it indefinite. *Metabolite Labs., Inc.*, 71 U.S.P.Q.2d at 1089.

Accordingly, the claim meets all three requirements for definiteness listed in MPEP §2173, as described in the legal precedent section above: (A) the present application discloses that the “intercalating moiety is preferably an aromatic molecule with an intercalative binding affinity for DNA” (Specification, para. [0009]); (B) the prior art, as evidenced by Long and Lerman, clearly define the intercalation as insertion of a molecule (such as a planar aromatic) into the DNA strands; and (3) Long and Lerman clearly show that one of ordinary skill in the art at the time of filing would have understood the meaning of “configured to insert into the structure of deoxyribonucleic acid.”

For at least the reasons discussed above, Applicants respectfully assert that independent claims 22 and 32 are not indefinite as written. Therefore, Applicants respectfully request withdrawal of the Examiner’s rejection of independent claims 22 and 32, and their respective dependent claims 23-31, 33-39, 43-48 and 50 under 35 U.S.C. § 112, second paragraph.

Claim Rejections under 35 U.S.C. § 102

In the Office Action, the Examiner rejected claims 22-29, 32-37 and 40-53 under 35 U.S.C. § 102(b) as being anticipated by Mattes. Applicants respectfully traverse this rejection.

Legal Precedent and Guidelines

Anticipation under section 102 can be found only if a single reference shows exactly what is claimed. *Titanium Metals Corp. v. Banner*, 778 F.2d 775, 227 U.S.P.Q. 773 (Fed. Cir. 1985). For a prior art reference to anticipate under section 102, every element of the claimed invention must be identically shown in a single reference. *In re Bond*, 910 F.2d 831, 15 U.S.P.Q.2d 1566 (Fed. Cir. 1990). To maintain a proper rejection under section 102, a single reference must teach each and every limitation of the rejected claim. *Atlas Powder v. E.I. du Pont*, 750 F.2d 1569 (Fed. Cir. 1984). Accordingly, the Applicants need only point to a single element not found in the cited reference to demonstrate that the cited reference fails to anticipate the claimed subject matter. The prior art reference also must show the identical invention "in as complete detail as contained in the ... claim" to support a *prima facie* case of anticipation. *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 U.S.P.Q. 2d 1913, 1920 (Fed. Cir. 1989).

Mattes does not disclose "a metal complexed with the intercalating moiety."

Turning now to the claims, independent claims 22, 32, 40 and 51 recite, *inter alia*, "a metal complexed with the intercalating moiety." Although Applicants do not intend or suggest that the specification should be read into the present claims, Applicants submit that the specification may be used as a guide for the claims. Examples of metals complexed with intercalating moieties are provided in Figs. 2 and 3, which clearly show that the intercalating moiety is part of a coordination complex attached to the metal species at multiple points (multi-dentate) to form a metal complex. The metal complexes thus formed are stable, both *in vitro* and *in vivo*. Specification, para. [0018]. The stability of the coordination complex allows generation of the complex at very low concentrations. *Id.* at para. [0019].

In contrast to the metal complexes recited in the present independent claims, Mattes teaches a "radiolabeled nucleic acid-targeting small molecule." Mattes, p. 6, ll. 14-16. The radiolabels on the small molecules of Mattes are not metal complexes, but are radioactive atoms covalently bound to a single carbon on the small molecule. *Id.* at col. 2, ll. 29-32

(which states that "a preferred form of the invention is a nucleic acid-binding or DNA-intercalating small molecule labeled with one or more of I¹²⁵, I¹³¹, and ³²P or both."). Further, Mattes states that the radiolabeled small molecules can be produced by standard oxidative iodination. *Id.* at col. 2, ll. 41-45. Although Mattes discloses a list of radionuclides, including two metals, which are claimed to work as radiolabels, Mattes discloses no multi-dentate ligands or synthesis procedures that may be used to form stable metal complexes with these metals. *Id.* at col. 2, l. 40.

Thus, Mattes does not disclose metal complexes, as recited in the present claims. Furthermore, the metal complexes recited by the present claims do not flow from the teachings of Mattes. Specifically, although radio-nuclides such as isotopes of iodine or phosphorous may be stable when bound to a single carbon, as disclosed in Mattes, one of ordinary skill in the art at the time of filing would not expect that the small molecules and synthesis procedures disclosed in Mattes would form metal complexes, as recited in the present claims. Finally, the one metal tested by Mattes, ¹¹¹In, was not disclosed as being part of a metal complex. *Id.* at col. 6, ll. 5-10; Table 1.

As noted in the legal precedent section, the reference must disclose the identical invention in as complete detail as in the claims to support a *prima facie* case for anticipation. *Richardson*, 9 U.S.P.Q.2d at 1920. As Mattes does not disclose "a metal complexed with the intercalating moiety," Mattes does not disclose all of the limitations of independent claims 22, 32, 40 and 51, and cannot anticipate these claims. For the same reasons, among others, Mattes cannot anticipate claims 23, 24, 26-29, 33-37, 41-50, 52 and 53, which depend from claims 22, 32, 40 and 51. Accordingly, Applicants respectfully request that the Examiner withdraw the rejections of these claims under 35 U.S.C. §102, and allow the claims to issue.

Claim Rejections under 35 U.S.C. § 103(a)

The Examiner rejected claims 30-31 and 38-39 under 35 U.S.C. § 103(a) as being unpatentable over Mattes in view of Holley et al. (Cancer Research 1992; 52: 4190-4195, hereinafter "Holley"). Applicants respectfully traverse these rejections.

Legal Precedent

Traditionally, to establish a *prima facie* case of obviousness, the CCPA and the Federal Circuit have required that the prior art not only include all of the claimed elements, but also some teaching, suggestion, or motivation to combine the known elements in the same manner set forth in the claim at issue. *See, e.g., ASC Hospital Systems Inc. v. Montifiore Hospital*, 221 U.S.P.Q. 929, 933 (Fed. Cir. 1984) (holding that obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention absent some teaching or suggestion supporting the combination.); *In re Mills*, 16 U.S.P.Q.2d 1430, 1433 (Fed. Cir. 1990) (holding that the mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. Accordingly, the first test for obviousness is whether the prior art references, either alone or in any sort of hypothetical combination, contain all of the elements of the present claims.

Mattes and Holley, taken alone or in hypothetical combination, fail to disclose a metal complex.

Turning to the claims, claims 30-31 ultimately depend from independent claim 22, while claims 38-39 ultimately depend from independent claim 32. The Examiner notes that “Mattes does not explicitly teach that tumor seeking molecule is spermidine.” Office Action, p. 6. However, the Examiner claims that the chlorambucil-spermidine conjugate of Holley would make the use of spermidine obvious. *Id.*

However, as discussed with respect to the rejection under 35 U.S.C. § 102, Mattes does not disclose “a metal complexed with the intercalating moiety,” as recited in claims 22 and 32. Furthermore, Holley, either individually, or in any sort of hypothetical combination with Mattes, does not obviate this deficiency.

Accordingly, independent claims 22 and 32 are allowable over Mattes in view of Holley. As claims 30 and 31 depend from claim 22 and claims 38 and 39 depend from claim 32, these claims are allowable for at least the same reasons as discussed above.

Therefore, Applicants respectfully request withdrawal of the rejection of claims 30, 31, 38 and 39 under 35 U.S.C. § 103.

Conclusion

Applicants respectfully submit that all pending claims should be in condition for allowance. However, if the Examiner believes certain amendments are necessary to clarify the present claims or if the Examiner wishes to resolve any other issues by way of a telephone conference, the Examiner is kindly invited to contact the undersigned attorney at the telephone number indicated below.

No fee is believed to be due for entry of this response. However, the Commissioner is hereby authorized to charge any fee deficiency to Deposit Account Number 13-1160.

Respectfully submitted,

A handwritten signature in black ink, appearing to read 'Anthony R. Kinney', is written over a horizontal line.

Anthony R. Kinney, Reg. No. 44,834
675 McDonnell Boulevard
Hazelwood, Missouri 63042
Telephone: (314) 654-8346
Fax: (314) 654-3156